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EXAMINER	
HORNING, MICHELLE S	

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1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,866	WERLING, DIRK	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2009 and 12 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,9-12,18,19,21-29,38,45-48,50 and 52-75* is/are pending in the application.

4a) Of the above claim(s) *12,22-29,45-48,50,55 and 60-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,9-11,18,19,21,38,52-54,56-59 and 69-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/8/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is responsive to communication 12/14/2009 and 1/12/2010. The status of the claims is as follows: claims 6, 9-11, 18, 19, 21, 38, 52-54, 56-59 and 69-75 are under current examination.

Claims 12, 22-29, 45-48, 50, 55 and 60-68 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/14/2009.

Applicant has elected the species F protein derived from RSV as the antigen (Response, filed 12/14/2009). Note that claims 12 and 55 do not read upon RSV and thus, are withdrawn.

Any rejection(s) and/or objection(s) not reiterated herein has been withdrawn.

To allow entry of the rejection(s) set forth herein, the instant office action is non-final.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See p. 10, line 6).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 9-11, 18, 19, 21, 38, 52-54, 56-59 and 69-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to (in part) an immunogenic compound comprising (i) HIV gp120, or parts thereof, and (ii) an antigen wherein the antigen is associated with a disease or part or variant thereof, wherein the antigen elicits an immune response to the disease (e.g. claim 6).

The following quotation from section 2163 of the MPEP is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed or

through disclosure of a functional characteristic of the claimed genus coupled with a known or disclosed non-functional characteristic (structure) that correlates to the function.

As noted above, the claims are drawn to (in part) an immunogenic compound comprising (i) HIV gp120, *or parts thereof*, and (ii) an antigen wherein the antigen is associated with a disease *or part or variant thereof*, wherein the antigen elicits an immune response to the disease (e.g. claim 6).

Structurally, the claims are broad and are drawn to any parts of HIV gp120 and any part or variant of the antigen. The instant specification discloses that the binding moiety, or gp120, selectively binds to and targets DC via the DC-SIGN receptor (p. 7, lines 4+ and p. 13, lines 17+, also see claim 69). While the instant specification provides two structural motifs possessed by a DC-SIGN receptor required for endocytosis, the specification fails to describe the required structural properties of gp120 and it is not clear what structural "parts" of this moiety would be required in order to successfully bind to DC-SIGN.

In view of a part of the antigen, the instant specification describes such a part may be as few as 5 amino acids and up to 100 amino acids (p. 12, lines 14+). A variant of the antigen includes an antigen comprising insertions, deletions and as many as 5% substitutions (p. 12-13). However, there is no written description demonstrating any antigen with insertions, deletions and substitutions so that the variant antigen may elicit *an immune response to the associated disease* as required by the instant claims. The instant specification also states the following: “It is necessary for endocytosis to occur

for an immune response to occur" (p. 34, lines 17). The specification fails to show which insertions, deletions and substitutions may occur in an antigen so that the necessary endocytosis may occur in order to gain an immune response.

The prior art provides that gp120 binds to dendritic cells via DC-SIGN receptors (Geijtenbeek et al., *J. Biol. Chem.*, 2002, IDS); however, the amino acids of gp120 involved in binding to this receptor has yet to mapped, including those that are directly or indirectly involved (e.g. downstream structural involvement, including structural stability). It is noted that gp120 comprises nearly 500 amino acids from which many "parts" comprising 5 to 100 amino acids may be derived (Kwong et al., *Nature*, 1998-attached; see Figure 2d, p. 651). Separately, Bowie et al. (*Science*, 1990-attached) teaches that structure prediction based from sequence and determination of function from structure are problems that have yet to be solved (p. 1306, col. 1). The authors also note that residues that are directly involved in protein function (e.g. binding) will be among the most conserved. However, to maintain protein function, the binding residues must be *precisely oriented* in three dimensions. Consequently, mutations in residues that are required for structure formation or stability can also have dramatic effects on activity (p. 1306, col. 2). The specification provides no written description which would support structure formation or gp120 stability in view of insertions, deletions and substitutions.

In view of a lack of structure to function correlations for *parts* of gp120 in receptor binding as well as for *a part or variant* of an antigen in the instant specification and the

lack of predictability as taught by the prior art in such protein structure to function correlations, the claims are rejected as lacking written description.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 9-11, 18, 38, 52-54, 56, 57 and 69-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Patterson et al. (*Biochem. and Biophys. Res. Com.,* 2001).

The claims are drawn to (in part) an immunogenic compound comprising (i) HIV gp120, or parts thereof, and (ii) an antigen wherein the antigen is associated with a disease or part or variant thereof, wherein the antigen elicits an immune response to the disease, wherein the gp120 and the antigen each comprise a polypeptide and both are present in the same polypeptide chain.

Patterson et al. describe a hybrid protein comprising hepatitis B core antigen linked to the amino end of large fragments of gp120 (see whole document; also see Figure 1, depicting different constructs; see claims 6, 52, 53 and 69). Note that this meets the limitations of a compound wherein the gp102 and antigen are present in the same polypeptide chain, wherein the gp120 and antigen are covalently linked (claim 56). Claims 9 and 54 read on the antigen comprising two or more molecules and because the HBcAg comprises more than two amino acids, this limitation is met. HBcAg

is associated with a disease and a pathogen, wherein the pathogen is a virus, meeting limitations of claims 9-11 and 71. Note that the authors provide that administration of this hybrid protein results in the production of antibodies (Figure 5), meeting the limitation of a vaccine (claims 18 and 70). The authors describe making antigen-gp120 hybrid on p. 640, col. 1 wherein the antigen and gp120 are co-expressed (claims 38 and 52).

Note that claim 69 is drawn to an immunogenic composition comprising a gp120 fused to a disease-associated polypeptide, wherein the gp120 "is able to bind the polypeptide to a DC-SIGN protein expressed at the surface of a dendritic cell of the animal" (lines 3-5). Although Patterson et al. does not provide that the disclosed hybrid protein meets this specific functional limitation; Patterson et al. meets the structural limitations of the claims. Thus, the structure must be at least capable of performing the claimed function, given a composition is inseparable from its properties. Also see MPEP 2112.01 II. COMPOSITION CLAIMS-IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES.

Separately, note that it is the immunogenic composition of claim 69 that claim 72 is drawn to as opposed to “a farm animal or a companion animal”.

The teachings of Patterson et al. anticipate the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19, 21, 58, 59 and 73-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patterson et al. (*Biochem. and Biophys. Res. Com.,* 2001) as applied to claims 6, 9-11, 18, 38, 52-54, 56, 57 and 69-72 above, and further in view of Hancock et al. (*Vaccine*, 2001).

The claims are further drawn to adjuvants, pharmaceutical carriers and using an F protein (RSV).

Patterson et al. teach a hybrid protein comprising a gp120 protein fragment fused to an HBcAg. The authors teach linking native gp120 to a potent immunogen to improve immunogenicity of gp120 vaccines in eliciting antibodies (p. 639, col. 1). The authors conclude that the disclosed hybrids should be a useful starting point for linking gp120 to a variety of carrier proteins capable of enhancing immunogenicity, while retaining the native structure needed to elicit broadly crossreactive neutralizing antibodies against HIV virus (p. 642, col. 2).

Patterson et al. does not teach using adjuvants (claims 19 and 58), pharmaceutical carriers (claims 21 and 59) and using an F protein derived from RSV as the antigen (claims 73-75).

Hancock et al. disclose using potent adjuvants in combination with an F protein of RSV as vaccines (whole document, claims 19, 58 and 73-75, in part). The authors vaccinated mice with a composition comprising an F protein and PBS in the presence or absence of CpG containing sequences and measured the resulting antibody titers (see

p. 4877, Table 1). Note that PBS meets the limitation of a pharmaceutical carrier (claims 21 and 59).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the F protein of RSV, a known and characterized immunogen, as an equivalent for HBcAg in the gp120-polypeptide hybrid as taught by Patterson et al. One would have been motivated to do so for the advantage of enhancing immunogenicity of gp120 vaccines as taught by Patterson et al.

It would have been obvious to one of ordinary skill in the art at the time of the invention to further use adjuvants for the advantage of amplifying an immune response (see Table 1 of Hancock et al.). Further, one of ordinary skill in the art would have been motivated to use a known pharmaceutical carrier, such as PBS, for the administration of the vaccine as taught by Hancock et al.

There would have been a reasonable expectation of success given the underlying techniques are widely known and commonly used as evidenced by the prior art (e.g. vaccination, making a hybrid protein etc.). The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zacharias Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
Primary Examiner, Art Unit 1648